

## MicroRNA-142 is a multifaceted regulator in organogenesis, homeostasis, and disease

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### Abstract

© 2016 Wiley Periodicals, Inc. Over the past decade, microRNA-142 (miR-142) is emerging as a major regulator of cell fate decision in the hematopoietic system. However, miR-142 is expressed in many other tissues, and recent evidence suggests that it may play a more pleiotropic role during embryonic development. In addition, miR-142 has been shown to play important functions in disease. miR-142 displays a functional role in cancer, virus infection, inflammation, and immune tolerance. Both a guide strand (miR-142-3p) and passenger strand (miR-142-5p) are generated from the miR-142 hairpin. miR-142-3p and -5p display overlapping but also independent target genes. Loss of function mouse models (genetrap, global knock out [KO], and conditional KO) have been reported and support the important role of miR-142 in different biological processes. This review will summarize the abundant literature already available for miR-142 and will lay the foundation for future works on this important microRNA. *Developmental Dynamics* 246:285–290, 2017. © 2016 Wiley Periodicals, Inc.

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### Keywords

development, disease, ERK, miR-142, stem cells, WNT signaling

### References

- [1] Ambros V, Lee RC. 2004. Identification of microRNAs and other tiny noncoding RNAs by cDNA cloning. *Methods Mol Biol* 265:131–158.
- [2] Annoni A, Brown BD, Cantore A, Sergi LS, Naldini L, Roncarolo MG. 2009. In vivo delivery of a microRNA-regulated transgene induces antigen-specific regulatory T cells and promotes immunologic tolerance. *Blood* 114:5152–5161.
- [3] Calin GA, Croce CM. 2006. MicroRNA signatures in human cancers. *Nat Rev Cancer* 6:857–866.
- [4] Carraro G, Shrestha A, Rostkovius J, Contreras A, Chao CM, El Agha E, Mackenzie B, Dilai S, Guidolin D, Taketo MM, Gunther A, Kumar ME, Seeger W, De Langhe S, Barreto G, Bellusci S. 2014. miR-142-3p balances proliferation and differentiation of mesenchymal cells during lung development. *Development* 141:1272–1281.
- [5] Chakkalakal JV, Jones KM, Basson MA, Brack AS. 2012. The aged niche disrupts muscle stem cell quiescence. *Nature* 490:355–360.
- [6] Chapnik E, Rivkin N, Mildner A, Beck G, Pasvolsky R, Metzl-Raz E, Birger Y, Amir G, Tirosh I, Porat Z, Israel LL, Lellouche E, Michaeli S, Lellouche JP, Izraeli S, Jung S, Hornstein E. 2014. miR-142 orchestrates a network of actin cytoskeleton regulators during megakaryopoiesis. *Elife* 3:e01964.
- [7] Chen CZ, Li L, Lodish HF, Bartel DP. 2004. MicroRNAs modulate hematopoietic lineage differentiation. *Science* 303:83–86.

- [8] Chen CZ, Schaffert S, Fragoso R, Loh C. 2013. Regulation of immune responses and tolerance: the microRNA perspective. *Immunol Rev* 253:112-128.
- [9] Chiou GY, Chien CS, Wang ML, Chen MT, Yang YP, Yu YL, Chien Y, Chang YC, Shen CC, Chio CC, Lu KH, Ma HI, Chen KH, Liu DM, Miller SA, Chen YW, Huang PI, Shih YH, Hung MC, Chiou SH. 2013. Epigenetic regulation of the miR142-3p/interleukin-6 circuit in glioblastoma. *Mol Cell* 52:693-706.
- [10] Danger R, Pallier A, Giral M, Martinez-Llordella M, Lozano JJ, Degauque N, Sanchez-Fueyo A, Soullillou JP, Brouard S. 2012. Upregulation of miR-142-3p in peripheral blood mononuclear cells of operationally tolerant patients with a renal transplant. *J Am Soc Nephrol* 23:597-606.
- [11] Deng B, Zhang Y, Zhang S, Wen F, Miao Y, Guo K. 2015. MicroRNA-142-3p inhibits cell proliferation and invasion of cervical cancer cells by targeting FZD7. *Tumour Biol* 36:8065-8073.
- [12] Friedman RC, Farh KK, Burge CB, Bartel DP. 2009. Most mammalian mRNAs are conserved targets of microRNAs. *Genome Res* 19:92-105.
- [13] Isobe T, Hisamori S, Hogan DJ, Zabala M, Hendrickson DG, Dalerba P, Cai S, Scheeren F, Kuo AH, Sikandar SS, Lam JS, Qian D, Dirbas FM, Somlo G, Lao K, Brown PO, Clarke MF, Shimon Y. 2014. miR-142 regulates the tumorigenicity of human breast cancer stem cells through the canonical WNT signaling pathway. *Elife* 3.
- [14] Iwasaki K, Yamamoto T, Inanaga Y, Hiramitsu T, Miwa Y, Murotani K, Narumi S, Watarai Y, Katayama A, Uchida K, Kobayashi T. 2016. MiR-142-5p and miR-486-5p as biomarkers for early detection of chronic antibody-mediated rejection in kidney transplantation. *Biomarkers*: 1-10.
- [15] Kaduthanam S, Gade S, Meister M, Brase JC, Johannes M, Dienemann H, Warth A, Schnabel PA, Herth FJ, Sultmann H, Muley T, Kuner R. 2013. Serum miR-142-3p is associated with early relapse in operable lung adenocarcinoma patients. *Lung Cancer* 80:223-227.
- [16] Kanehira M, Kikuchi T, Santoso A, Tode N, Hirano T, Ohkouchi S, Tamada T, Sugiura H, Harigae H, Ichinose M. 2014. Human marrow stromal cells downsize the stem cell fraction of lung cancers by fibroblast growth factor 10. *Mol Cell Biol* 34:2848-2856.
- [17] Kramer NJ, Wang WL, Reyes EY, Kumar B, Chen CC, Ramakrishna C, Cantin EM, Vonderfecht SL, Taganov KD, Chau N, Boldin MP. 2015. Altered lymphopoiesis and immunodeficiency in miR-142 null mice. *Blood* 125:3720-3730.
- [18] Lagos-Quintana M, Rauhut R, Lendeckel W, Tuschl T. 2001. Identification of novel genes coding for small expressed RNAs. *Science* 294:853-858.
- [19] Lau NC, Lim LP, Weinstein EG, Bartel DP. 2001. An abundant class of tiny RNAs with probable regulatory roles in *Caenorhabditis elegans*. *Science* 294:858-862.
- [20] Lei Z, Xu G, Wang L, Yang H, Liu X, Zhao J, Zhang HT. 2014. MiR-142-3p represses TGF-beta-induced growth inhibition through repression of TGFbetaR1 in non-small cell lung cancer. *FASEB J* 28:2696-2704.
- [21] Lin RJ, Xiao DW, Liao LD, Chen T, Xie ZF, Huang WZ, Wang WS, Jiang TF, Wu BL, Li EM, Xu LY. 2012. MiR-142-3p as a potential prognostic biomarker for esophageal squamous cell carcinoma. *J Surg Oncol* 105:175-182.
- [22] Lu X, Li X, He Q, Gao J, Gao Y, Liu B, Liu F. 2013. miR-142-3p regulates the formation and differentiation of hematopoietic stem cells in vertebrates. *Cell Res* 23:1356-1368.
- [23] Ma Z, Liu T, Huang W, Liu H, Zhang HM, Li Q, Chen Z, Guo AY. 2016. MicroRNA regulatory pathway analysis identifies miR-142-5p as a negative regulator of TGF-beta pathway via targeting SMAD3. *Oncotarget* doi: 10.18632/oncotarget.
- [24] Morimoto T, Sunagawa Y, Kawamura T, Takaya T, Wada H, Nagasawa A, Komeda M, Fujita M, Shimatsu A, Kita T, Hasegawa K. 2008. The dietary compound curcumin inhibits p300 histone acetyltransferase activity and prevents heart failure in rats. *J Clin Invest* 118:868-878.
- [25] Nardiello C, Morty RE. 2016. MicroRNA in late lung development and bronchopulmonary dysplasia: the need to demonstrate causality. *Mol Cell Pediatr* 3:19.
- [26] Nimmo R, Ciau-Uitz A, Ruiz-Herguido C, Soneji S, Bigas A, Patient R, Enver T. 2013. MiR-142-3p controls the specification of definitive hemangioblasts during ontogeny. *Dev Cell* 26:237-249.
- [27] Nishiyama T, Kaneda R, Ono T, Tohyama S, Hashimoto H, Endo J, Tsuruta H, Yuasa S, Ieda M, Makino S, Fukuda K. 2012. miR-142-3p is essential for hematopoiesis and affects cardiac cell fate in zebrafish. *Biochem Biophys Res Commun* 425:755-761.
- [28] Obernosterer G, Leuschner PJ, Alenius M, Martinez J. 2006. Post-transcriptional regulation of microRNA expression. *RNA* 12:1161-1167.
- [29] Schulte C, Zeller T. 2015. microRNA-based diagnostics and therapy in cardiovascular disease-Summing up the facts. *Cardiovasc Diagn Ther* 5:17-36.
- [30] Sharma S, Liu J, Wei J, Yuan H, Zhang T, Bishopric NH. 2012. Repression of miR-142 by p300 and MAPK is required for survival signalling via gp130 during adaptive hypertrophy. *EMBO Mol Med* 4:617-632.
- [31] Shrestha A, Carraro G, El Agha E, Mukhametshina R, Chao CM, Rizvanov A, Barreto G, Bellusci S. 2015. Generation and validation of miR-142 knock out mice. *PLoS One* 10:e0136913.

- [32] Sladitschek HL, Neveu PA. 2015. The bimodally expressed microRNA miR-142 gates exit from pluripotency. *Mol Syst Biol* 11:850.
- [33] Sun Y, Varambally S, Maher CA, Cao Q, Chockley P, Toubai T, Malter C, Nieves E, Tawara I, Wang Y, Ward PA, Chinnaiyan A, Reddy P. 2011. Targeting of microRNA-142-3p in dendritic cells regulates endotoxin-induced mortality. *Blood* 117:6172–6183.
- [34] Tsang FH, Au SL, Wei L, Fan DN, Lee JM, Wong CC, Ng IO, Wong CM. 2015. MicroRNA-142-3p and microRNA-142-5p are downregulated in hepatocellular carcinoma and exhibit synergistic effects on cell motility. *Front Med* 9:331–343.
- [35] Vegter EL, van der Meer P, de Windt LJ, Pinto YM, Voors AA. 2016. MicroRNAs in heart failure: from biomarker to target for therapy. *Eur J Heart Fail* 18:457–468.
- [36] Wang XS, Gong JN, Yu J, Wang F, Zhang XH, Yin XL, Tan ZQ, Luo ZM, Yang GH, Shen C, Zhang JW. 2012. MicroRNA-29a and microRNA-142-3p are regulators of myeloid differentiation and acute myeloid leukemia. *Blood* 119:4992–5004.
- [37] Wei JQ, Shehadeh LA, Mitrani JM, Pessanha M, Slepak TI, Webster KA, Bishopric NH. 2008. Quantitative control of adaptive cardiac hypertrophy by acetyltransferase p300. *Circulation* 118:934–946.
- [38] Wu L, Cai C, Wang X, Liu M, Li X, Tang H. 2011. MicroRNA-142-3p, a new regulator of RAC1, suppresses the migration and invasion of hepatocellular carcinoma cells. *FEBS Lett* 585:1322–1330.